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Blood Cancers

What to Expect and What is New

Raya Mawad, MD
Swedish Cancer Institute
Seattle, WA


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DR. JONES
EYE.
EAR.
NOSE
AND
THROAT
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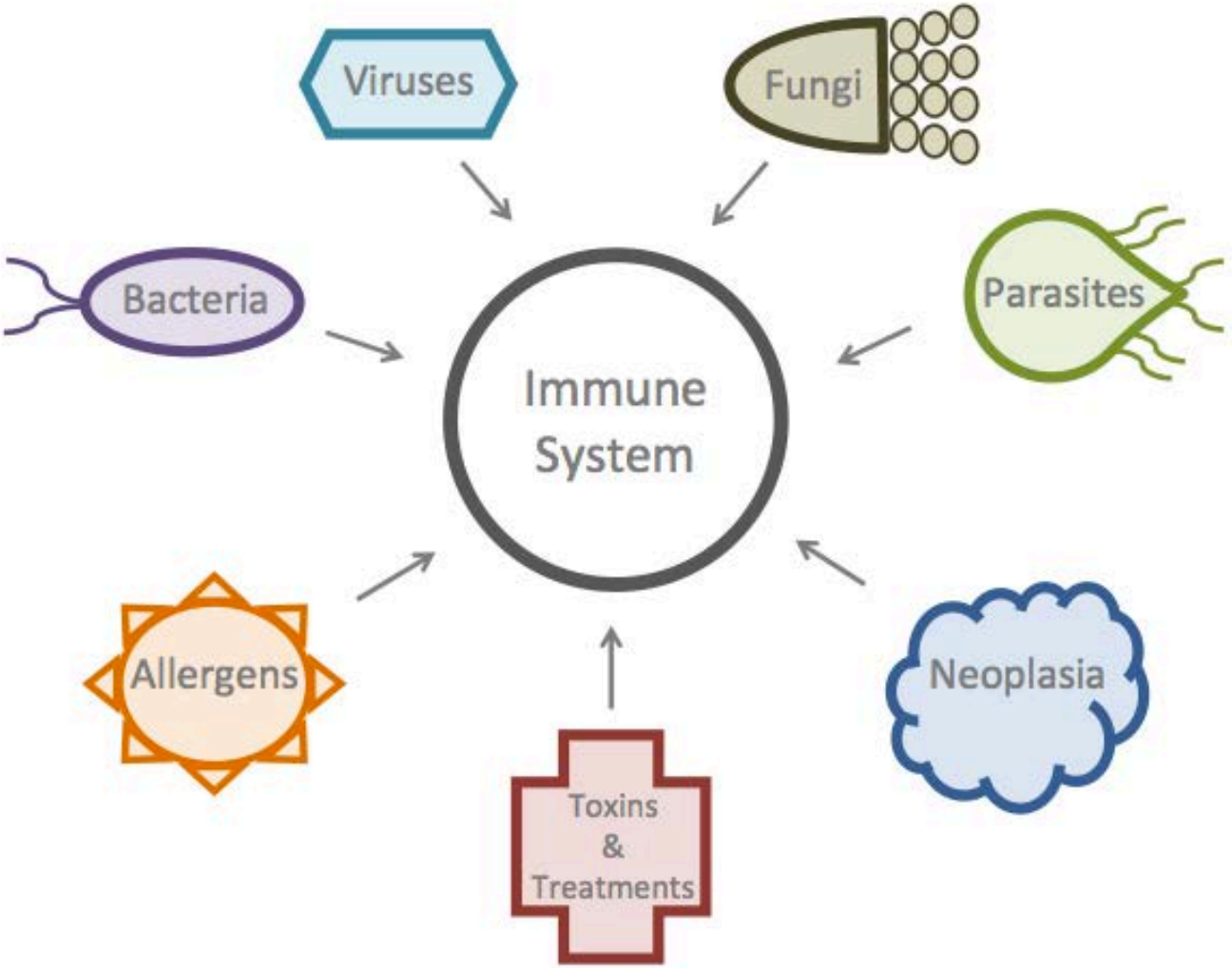
Viruses
Fungi
Bacteria
Parasites
Immune System
Allergens
Neoplasia
Toxins & Treatments

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What is Blood Cancer?

Cancer of certain types of blood cells:

- -Myeloid Cells
  - -Myelodysplastic Syndrome (MDS)
  - -Acute Myeloid Leukemia (AML)
  - -Chronic Myeloid Leukemia (CML)
- -Lymphoid Cells:
  - -Lymphoma
  - -Chronic Lymphoid Leukemia (CLL)
  - -Acute Lymphoid Leukemia (ALL)
- Plasma cells:
  - -MGUS
  - -Multiple Myeloma

Organs of the Immune System

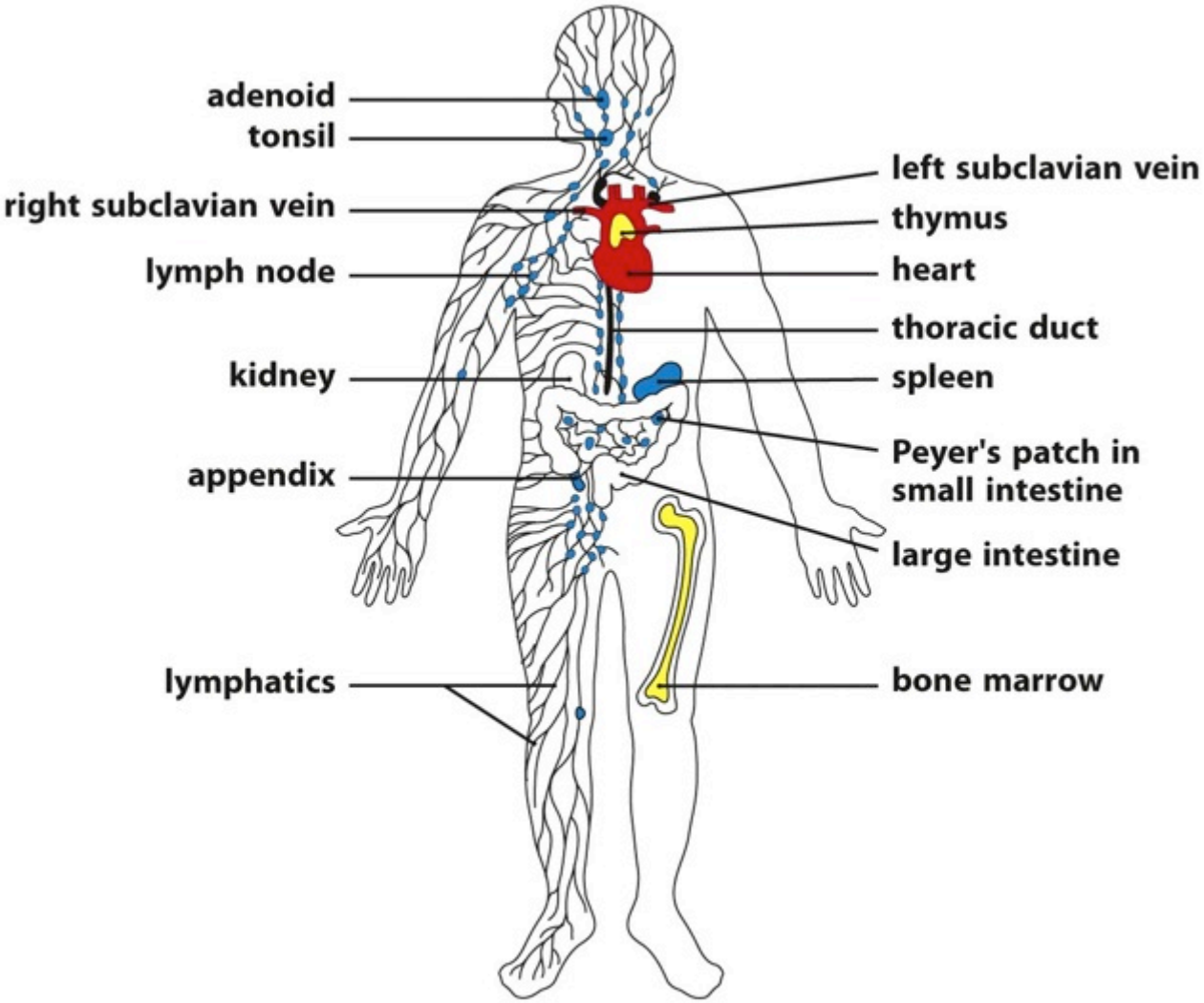
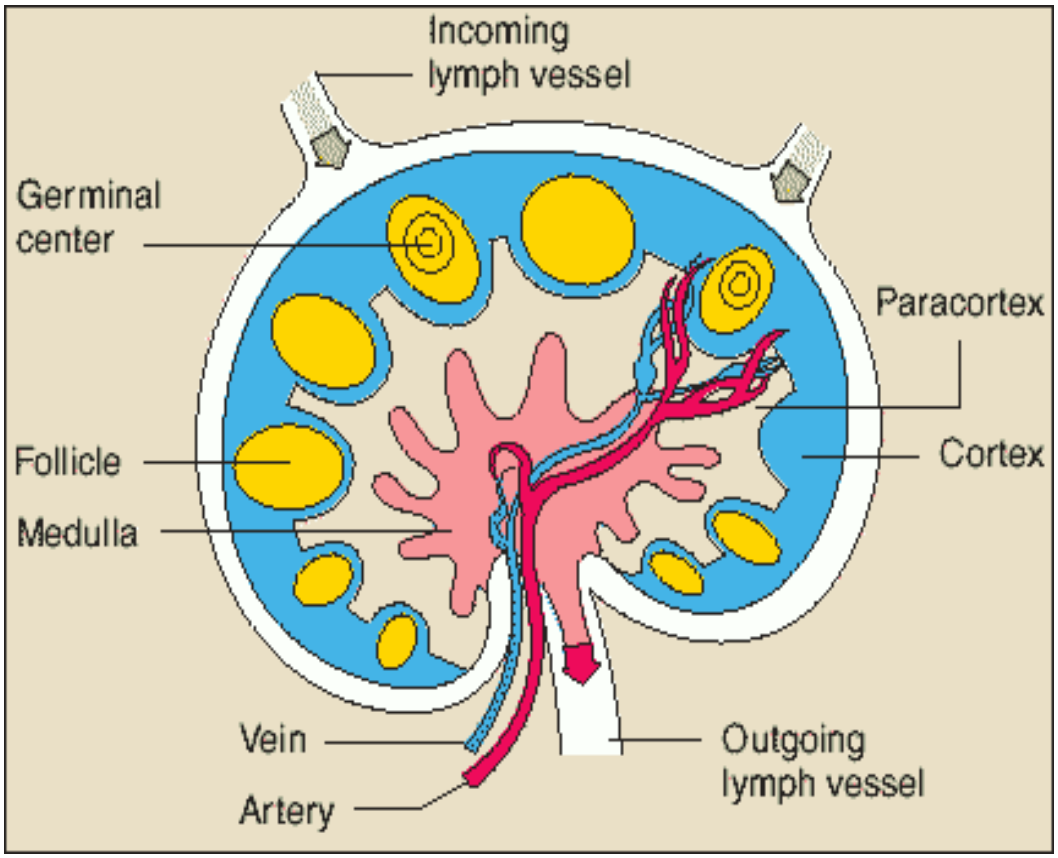
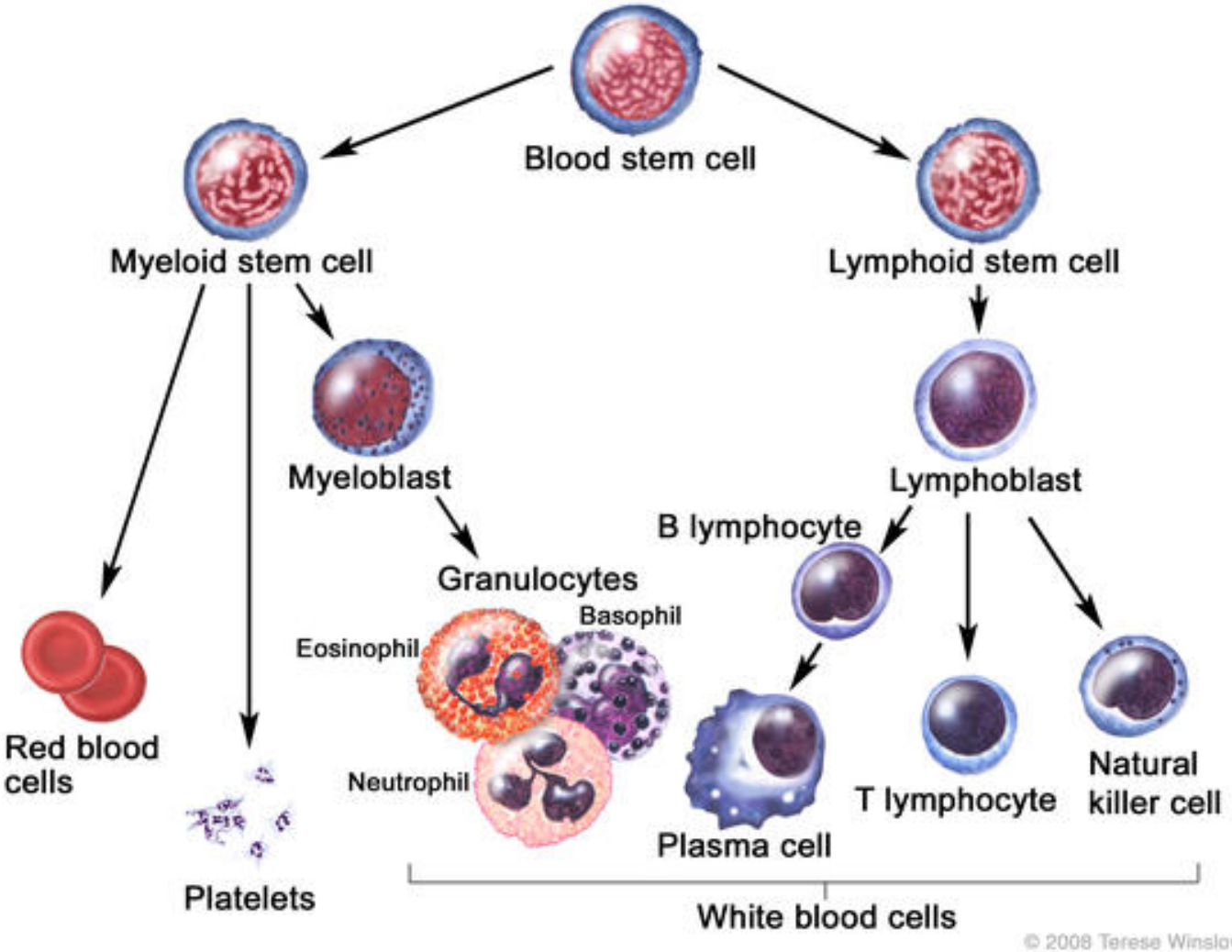


Figure 1.8 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Anatomy of a Lymph Node





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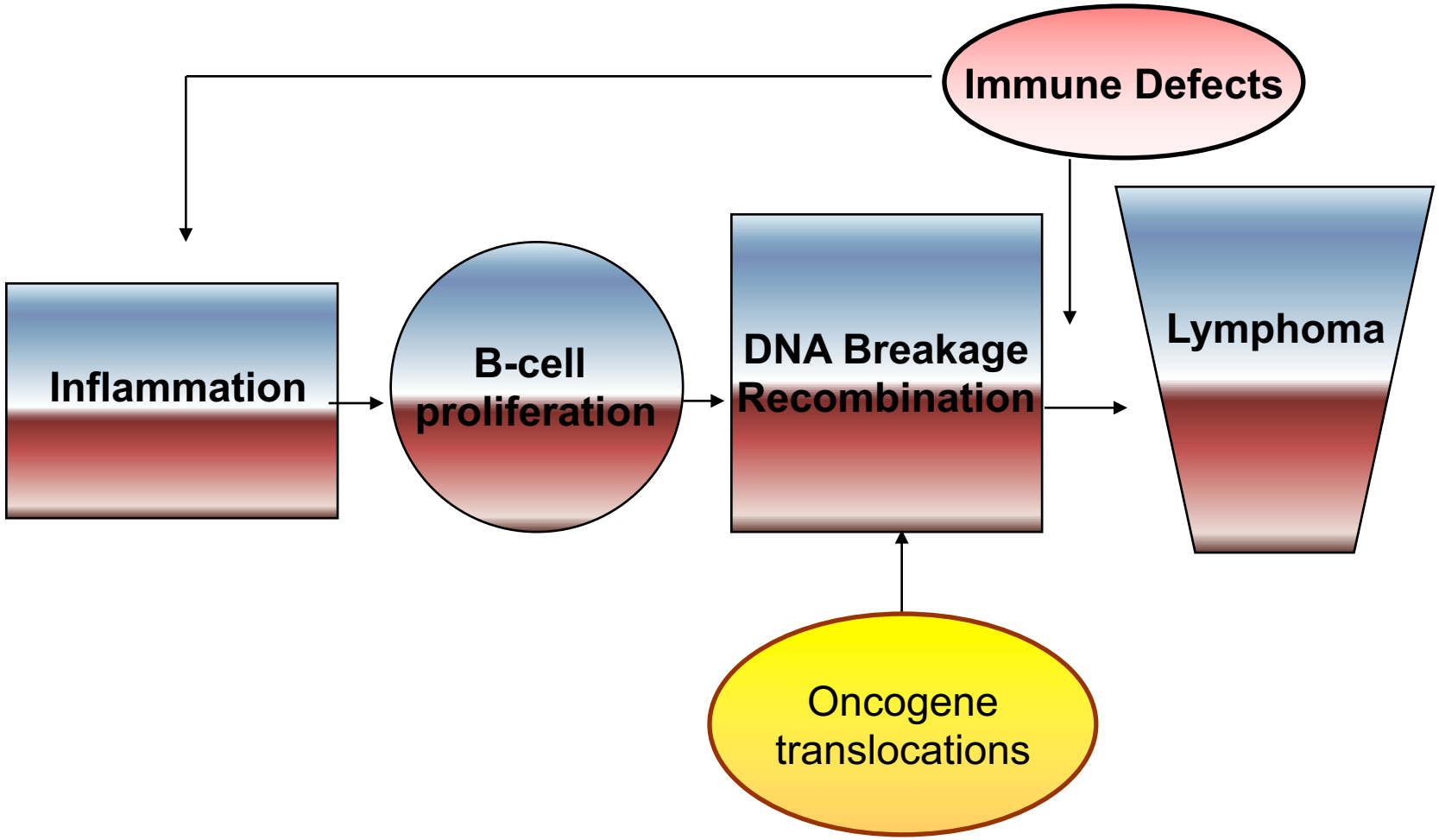
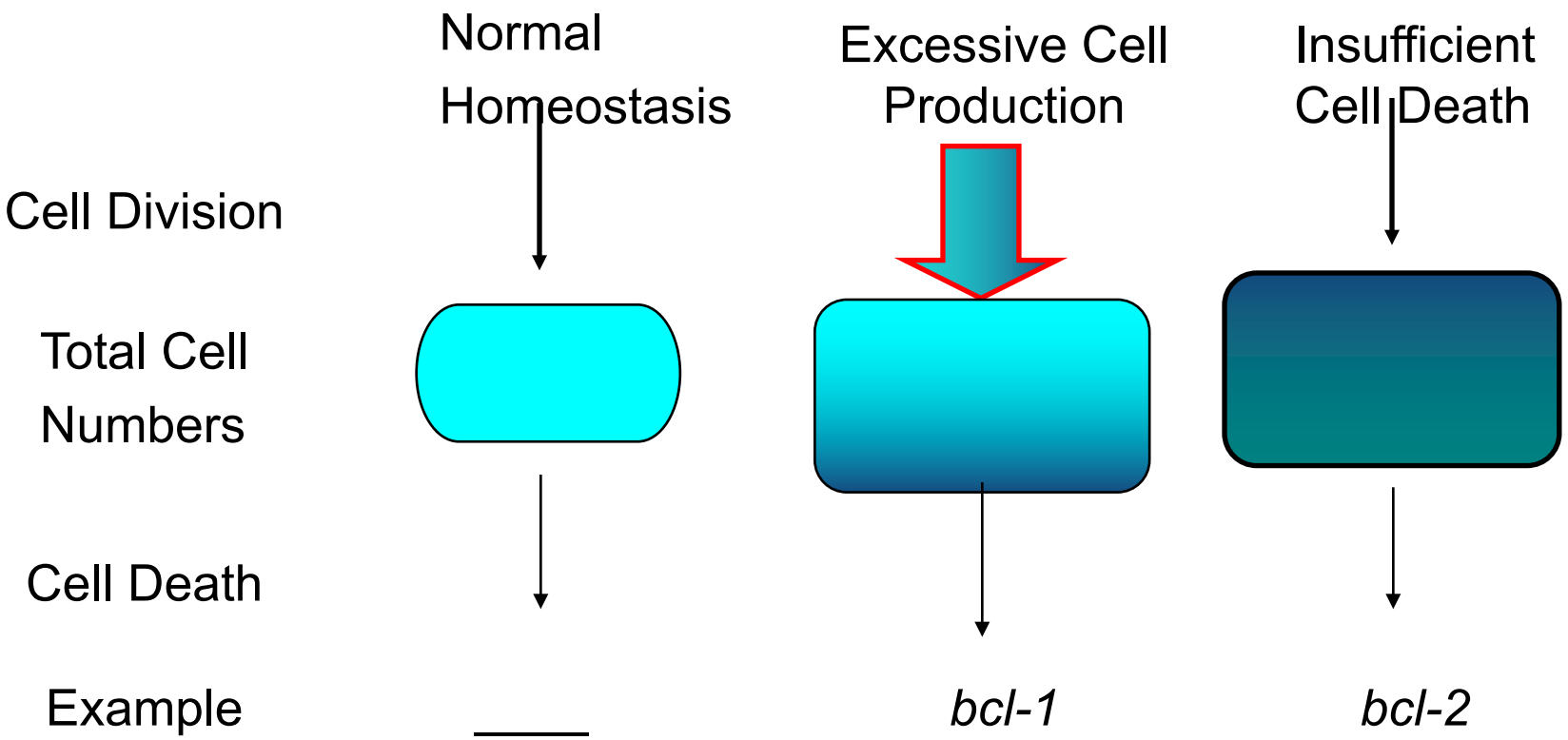


Lymphomagenesis in Autoimmune Diseases

Balancing Cell Production With Cell Death



Courtesy of John C. Reed, MD, PhD

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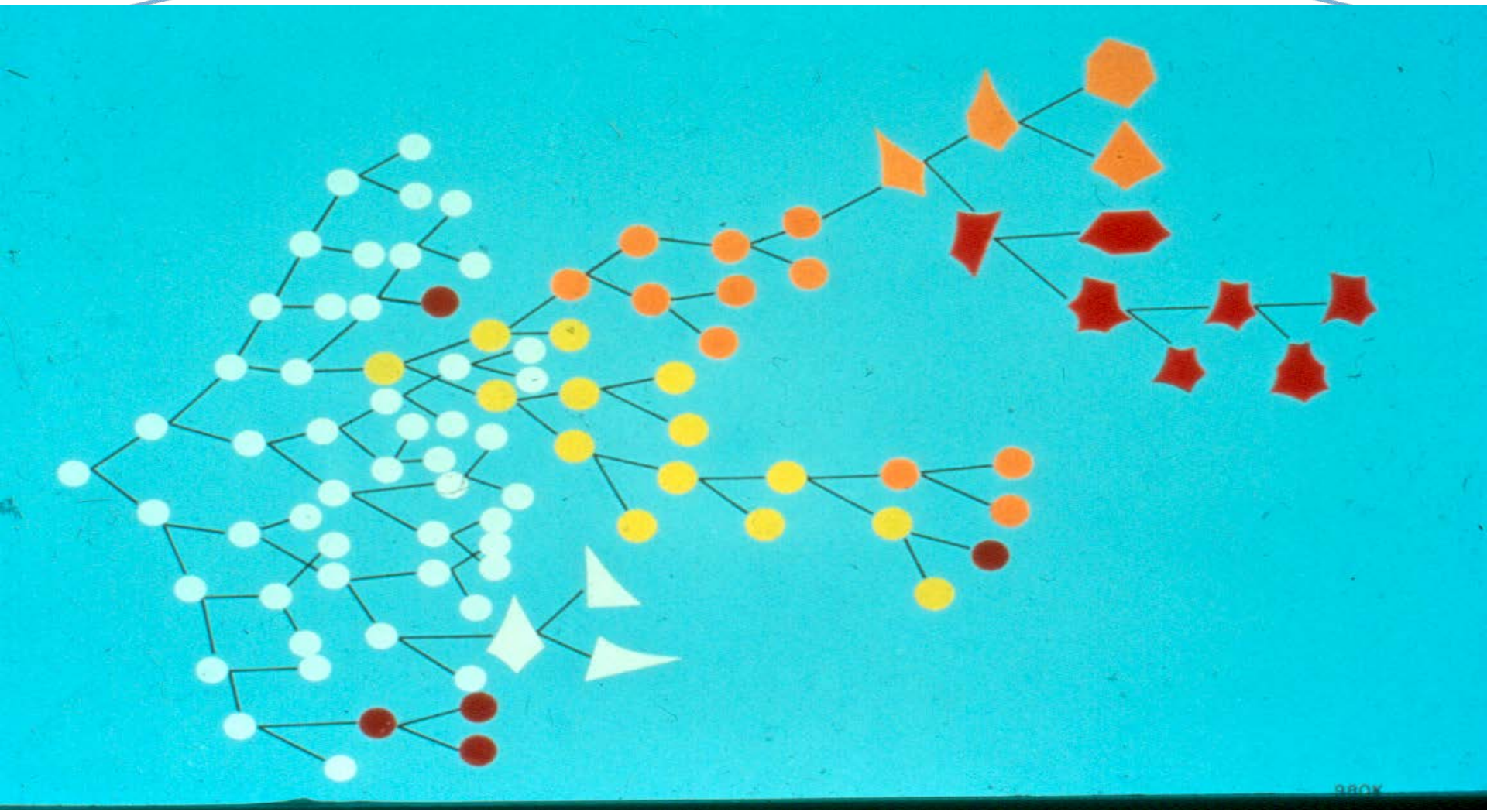
Tumor Progression & Clonal Evolution



Courtesy of T. Miller, MD

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Lymphoma, Leukemia & Myeloma Symptoms

Swelling of lymph nodes (Lymphoma or lymphoid leukemia)

-often, but not always painless

Fever

Drenching Night sweats

Unexplained weight loss (> 10% baseline in a few months)

Lack of energy

Low blood counts or abnormally high white blood count

Recurrent or Persistent infection (leukemia)

Bone Pain

Fractures or bone abnormalities on imaging

Risk Factors

Immunodeficiency disorders

Autoimmune disorders

Organ transplantation (immunosuppressed)

Chemical or pesticide exposure (high level benzene, chemo)

Radiation exposure (atomic bomb survivors)

Bacteria or viruses (HIV, Hepatitis, EBV, HTLV-1, H. pylori)

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Lymphoma Staging

Stage I - Cancer is found only in a single lymph node or in one organ or area outside the lymph node

Stage II - Cancer is found in two or more lymph nodes regions on one side of the diaphragm

Stage III - Cancer involves lymph nodes above and below the diaphragm

Stage IV - Cancer is found in several parts of one or more organs or tissues (in addition to the lymph nodes); or, it is in the liver, blood or bone marrow

Lymphoma Prognosis & Characterization

How fast is the lymphoma growing? Is it aggressive?

What Stage lymphoma?

Patient age & functional status

Genetics and surface protein expression of lymphoma cells

Leukemia Prognosis/Characterization

Chronic vs Acute

Lymphoid or Myeloid

Percentage of leukemia cells (blasts) in bone marrow

What are the other blood counts

What are the genetic mutations in the leukemia cells

Myeloma

Percentage of plasma cells in bone marrow

How high is the abnormal protein made by those plasma cells

Any end organ involvement (bone lesions, low blood counts, kidneys affected, high calcium)

Genetics of the plasma cells

Diagnosis

Physical examination

> Enlarged lymph node or spleen

Biopsy

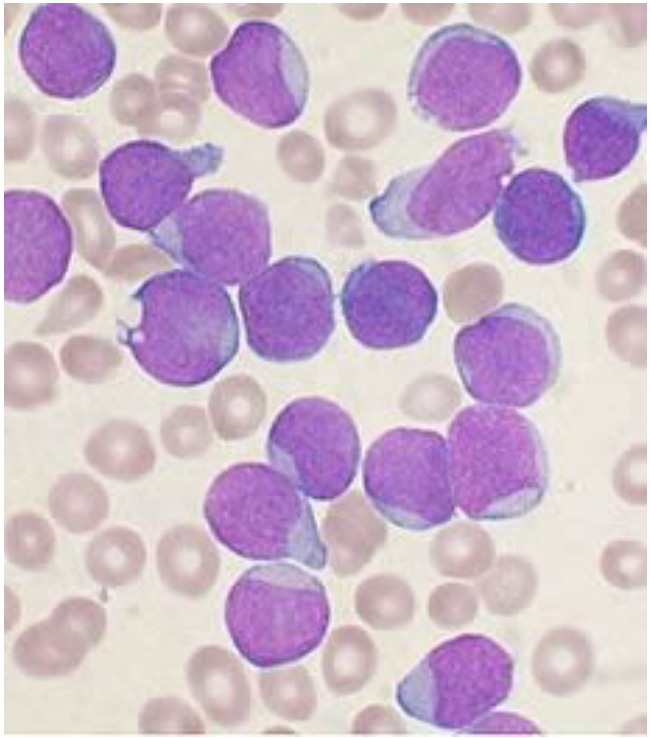
> Adequate tissue imperative
> Excisional node biopsy (optimal)
> Bone Marrow biopsy (leukemia, myeloma & often lymphoma)
> Fine needle aspiration is often inadequate for lymphoma

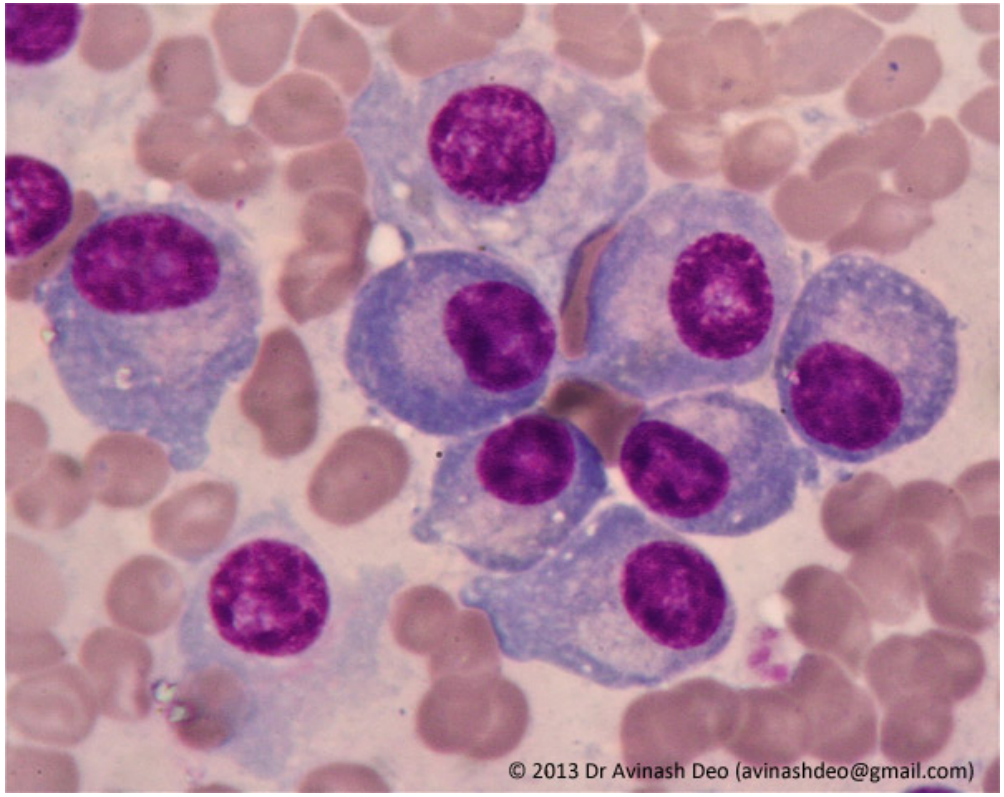
Adequate immunophenotyping

> Immunohistochemistry to look at surface protein expression
> Flow cytometry to detect cell surface markers

Cytogenetics/FISH to detect genetic abnormalities when appropriate

Acute leukemia or Myeloma





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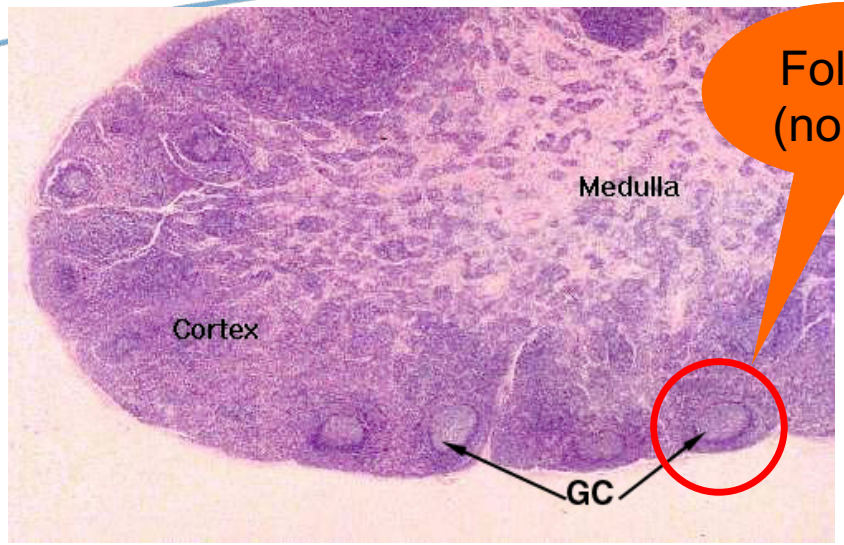
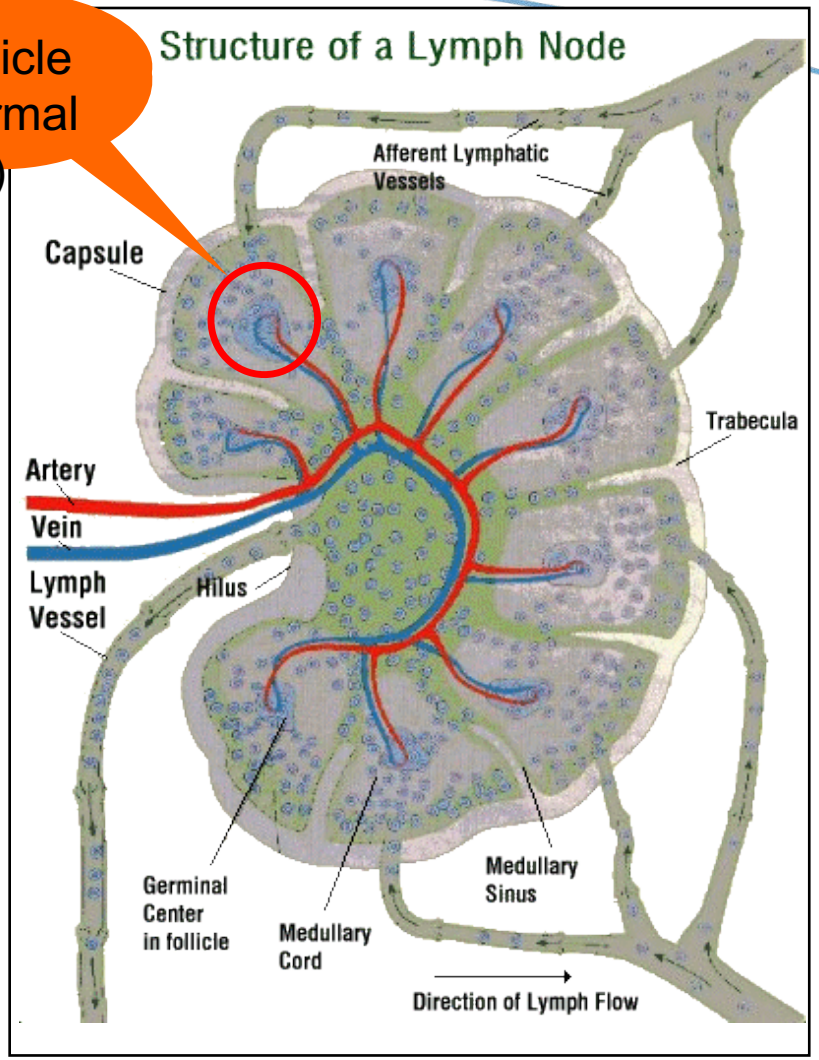
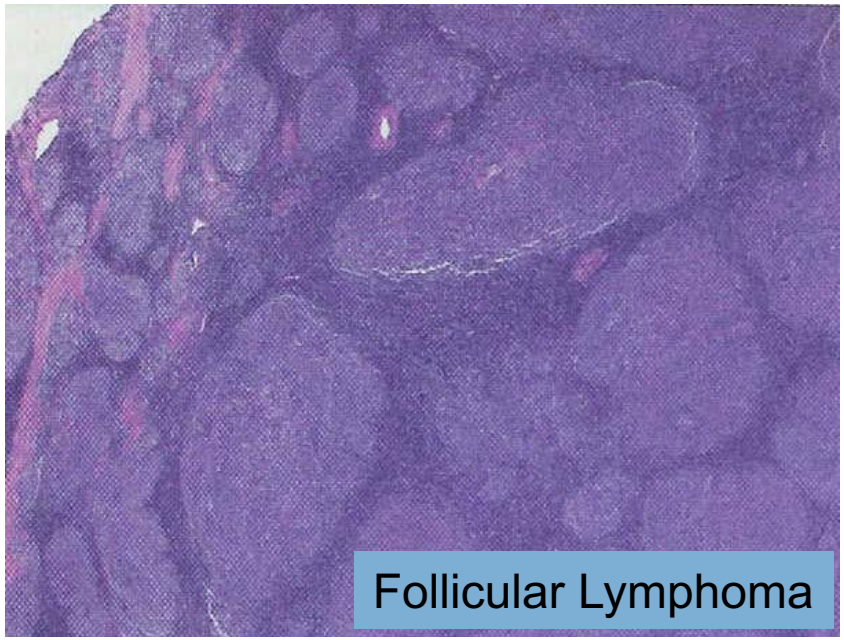
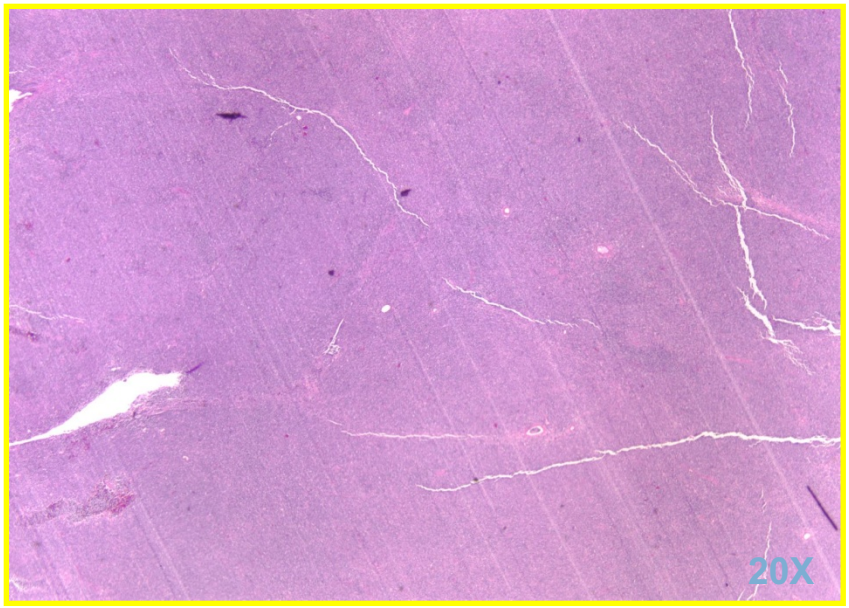
Follicular lymphoma

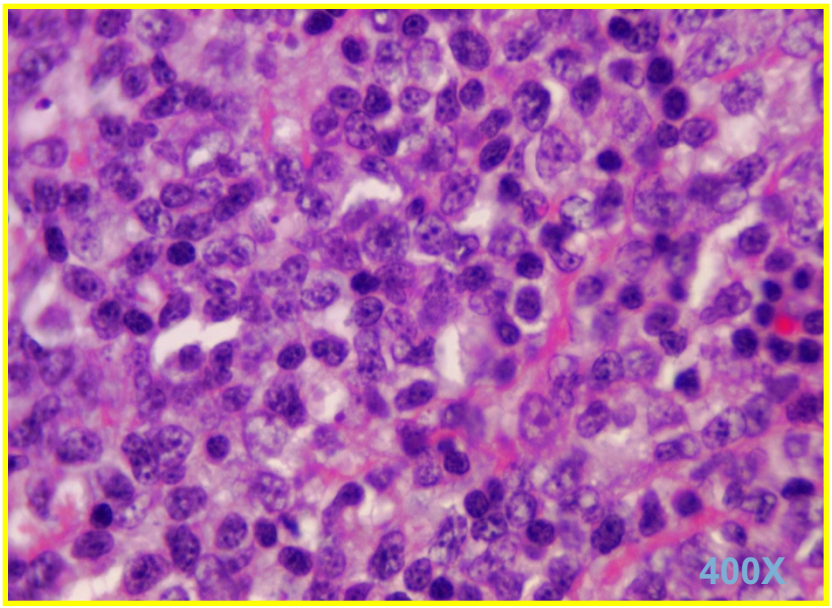






Diffuse Large B Cell Lymphoma





The lymph node has solid sheets of large malignant looking lymphocytes. Relatively fast growing.

Lymphoma Staging Evaluation

History and complete physical examination

Laboratory evaluation

> Standard blood studies

- Complete blood count, differential blood count, blood smear examination
- LDH and β2-microglobulin
- Liver function tests
- Renal function tests
- Serum electrolyte, calcium and uric acid levels

Bone marrow

> Leukemia, myeloma & many lymphomas

Radiologic studies

> CT scans (abdomen, pelvis and thorax)/PET in selected histology's

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WHO Classification of B-Cell Neoplasms

Precursor B-cell neoplasm

- Precursor B-lymphoblastic leukemia/lymphoma (precursor B-cell acute lymphoblastic leukemia)

Mature (peripheral) B-cell neoplasms

- B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma
- B-cell prolymphocytic leukemia
- Lymphoplasmacytic lymphoma
- Splenic marginal zone B-cell lymphoma (with or w/o villous lymphocytes)
- Hairy cell leukemia
- Plasma cell myeloma/plasmacytoma
- Extranodal marginal zone B-cell lymphoma of mucosa- associated lymphoid tissue type
- Nodal marginal zone B-cell lymphoma (with or w/o monocytoid B cells)
- Follicular lymphoma
- Mantle cell lymphoma
- Diffuse large B-cell lymphoma
- Mediastinal large B-cell lymphoma
- Primary effusion lymphoma
- Burkitt's lymphoma/Burkitt's cell leukemia

Harris et al. *Hematol J.* 2000;1:53.

How Does One Decide Which Treatment to Recommend?

Classification

> Subtype

Growth rate (grade)

> Indolent vs. Aggressive

Stage of disease

> Local, distant, widespread

Prognostic Factors

> IPI, FLIPI, MIPI

Other factors

Treatment Options

Watchful waiting:

-slow growing (indolent) lymphomas

- low risk, early MDS (precursor to AML)

-low risk MGUS (precursor to myeloma)

Chemotherapy: various DNA damaging agents (usually through IV)

Radiation therapy (lymphoma or myeloma)

Immunotherapy and targeted agents

Stem cell transplantation

Watchful Waiting

Often for indolent low-grade NHLs

Low risk, early MDS (precursor to AML)

Low risk MGUS (precursor to myeloma)

> Regular physical exam and lab evaluation

> No treatment until patient has:

- Symptoms- fever, chills, night sweats, weight loss
- Signs the disease is progressing
- lower blood counts, worsening kidney function

> Treatment of indolent lymphoma at diagnosis does not improve survival or decrease incidence of transformation to a more aggressive lymphoma

Chemotherapy (Chemo)

Various drugs that affect DNA replication & cell growth

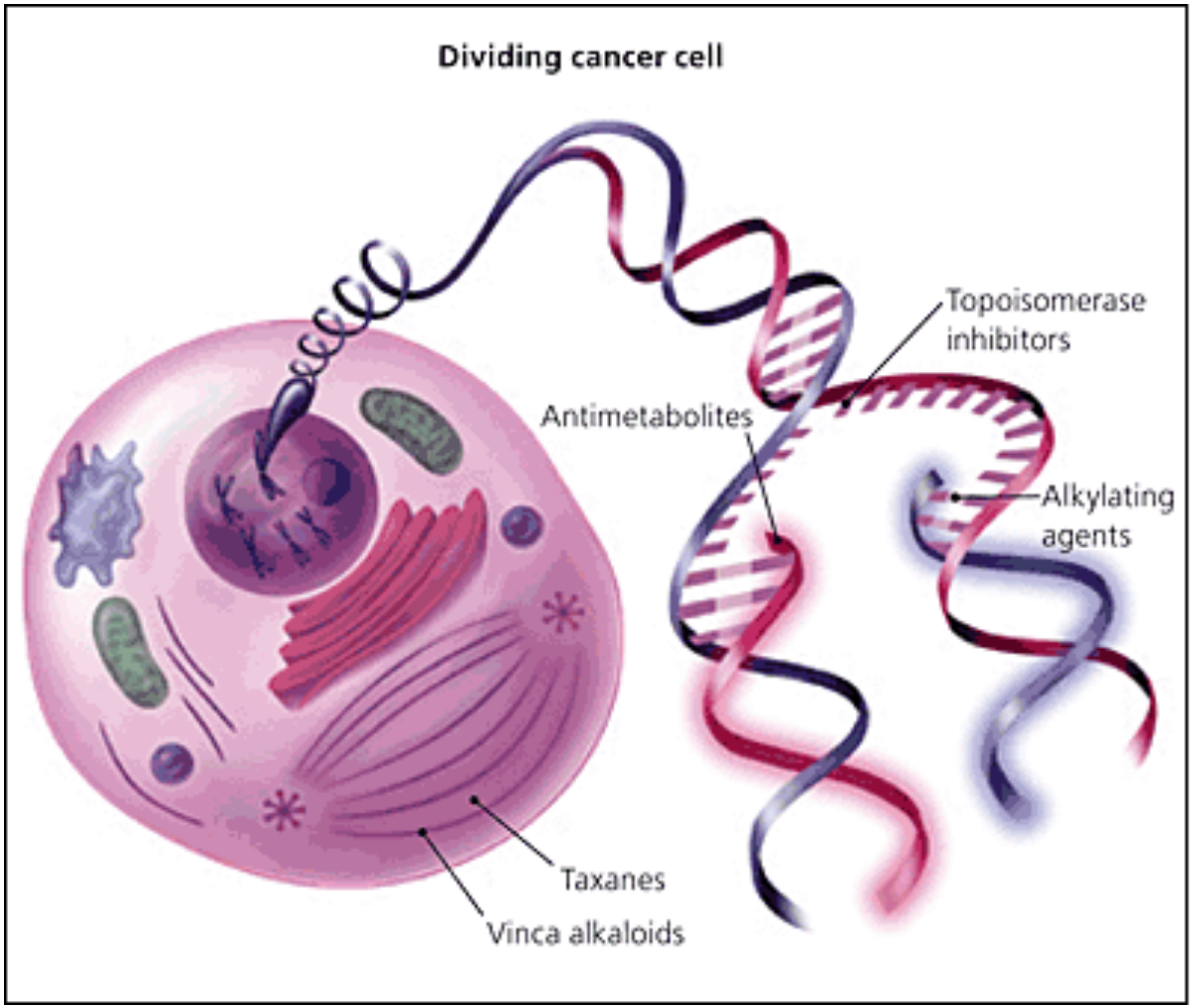
Different administration, schedule & side effects

Often given in combination

Often given IV and requires central venous access

-PORT or PICC or Hickman

Chemotherapy



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Chemo Side Effects

Non-drug specific

- Fatigue, loss of appetite, low energy
- Nausea, vomiting, diarrhea
- Low blood counts
  - White cells: risk of infections
  - Platelets: risk of bruising/bleeding
  - Red cells: anemia
- Hair loss, skin and nail changes

Chemo agent-specific

- Doxorubicin- heart toxicity (heart failure)
- Vincristine- nerve ending toxicity (neuropathy)
- Prednisone- high blood sugar, agitation, loss of sleep, stomach irritation, “shakiness”

Radiation Therapy

Used primarily in early stage lymphomas

Can be used for palliative (symptom) therapy

Acute side effects

> Nausea/vomiting, inflammation, fatigue, pain

Long term side effects

> Risk of secondary cancers, risk of marrow failure, risk of heart disease and pulmonary fibrosis

Usually combined with chemotherapy

External Beam Radiation

Stem Cell Transplantation

-Autologous vs Allogeneic

- Autologous: used in relapsed lymphomas or up front in some aggressive lymphomas and in myeloma
  - Used as a rescue to allow high doses of chemotherapy

- Allogeneic: used in more in leukemia & later in relapsed lymphoma
  - Used as a rescue
  - Uses the Graft versus Leukemia/Lymphoma (GvL) effect
  - Bone Marrow vs Peripheral Blood vs Cord Blood
  - Various Donor options (related vs unrelated donors)
  - Myeloablative vs Reduced Intensity conditioning prior to stem cell infusion

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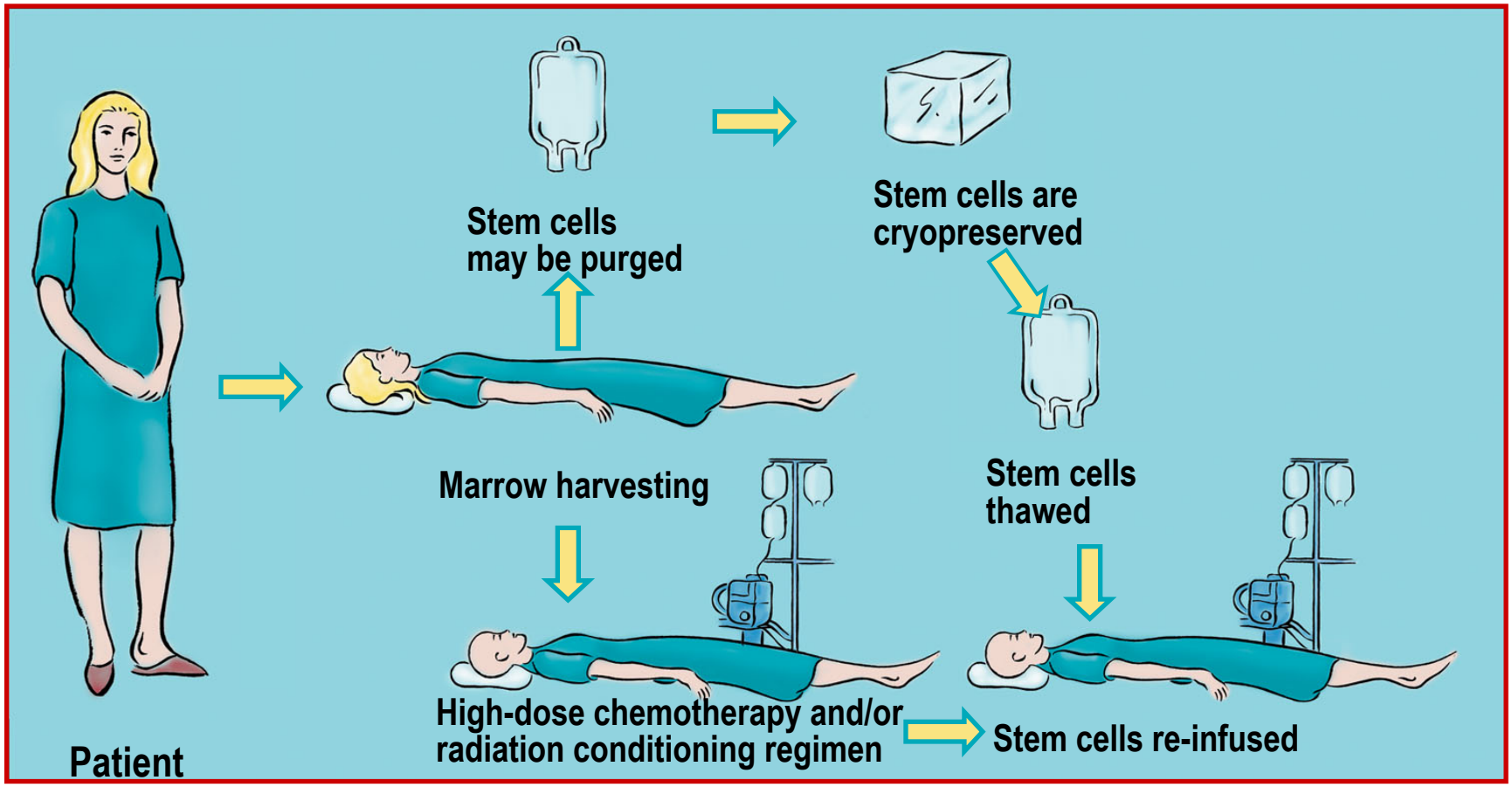
Autologous Stem Cell Transplant: Procedure Overview



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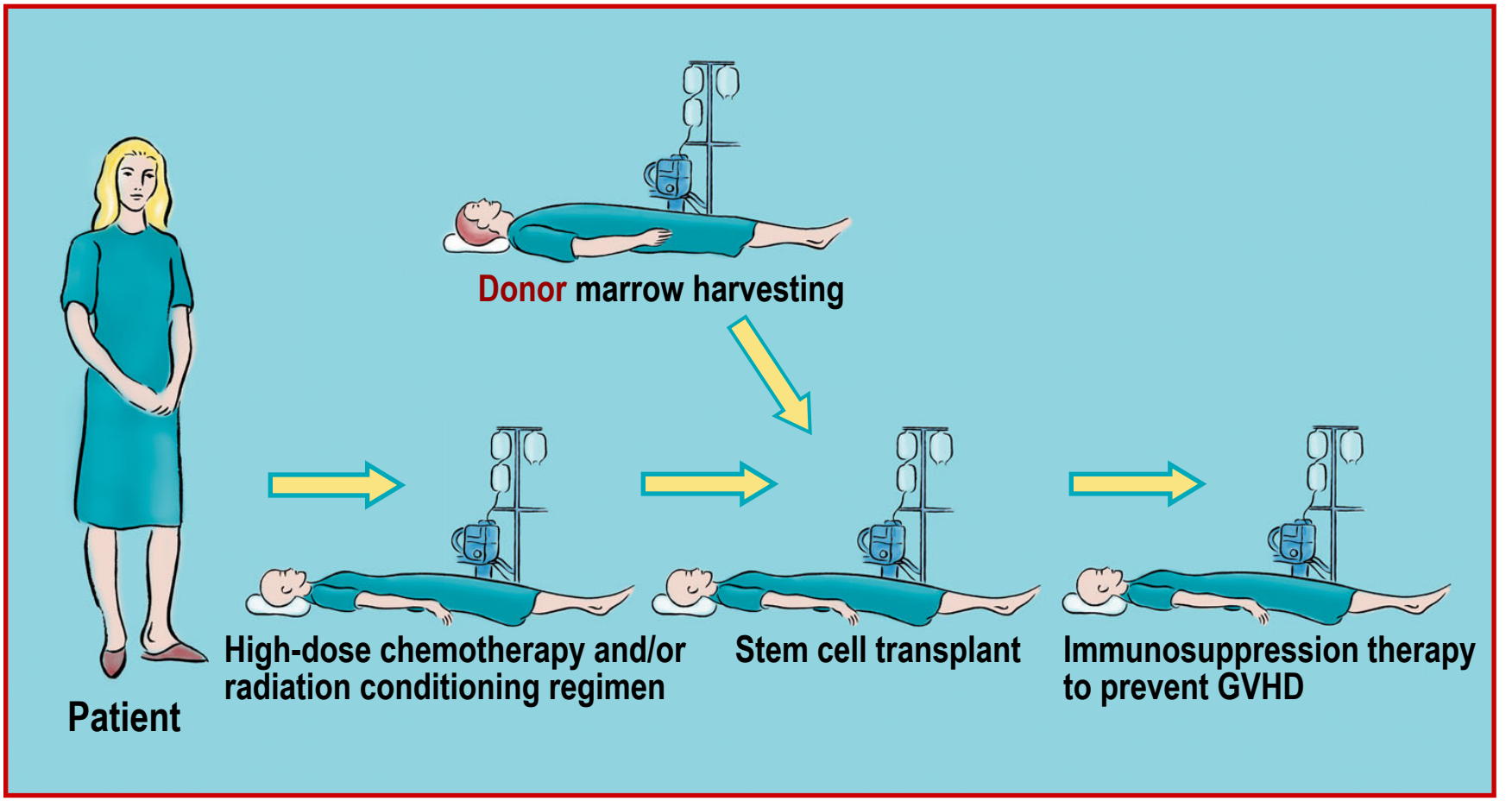
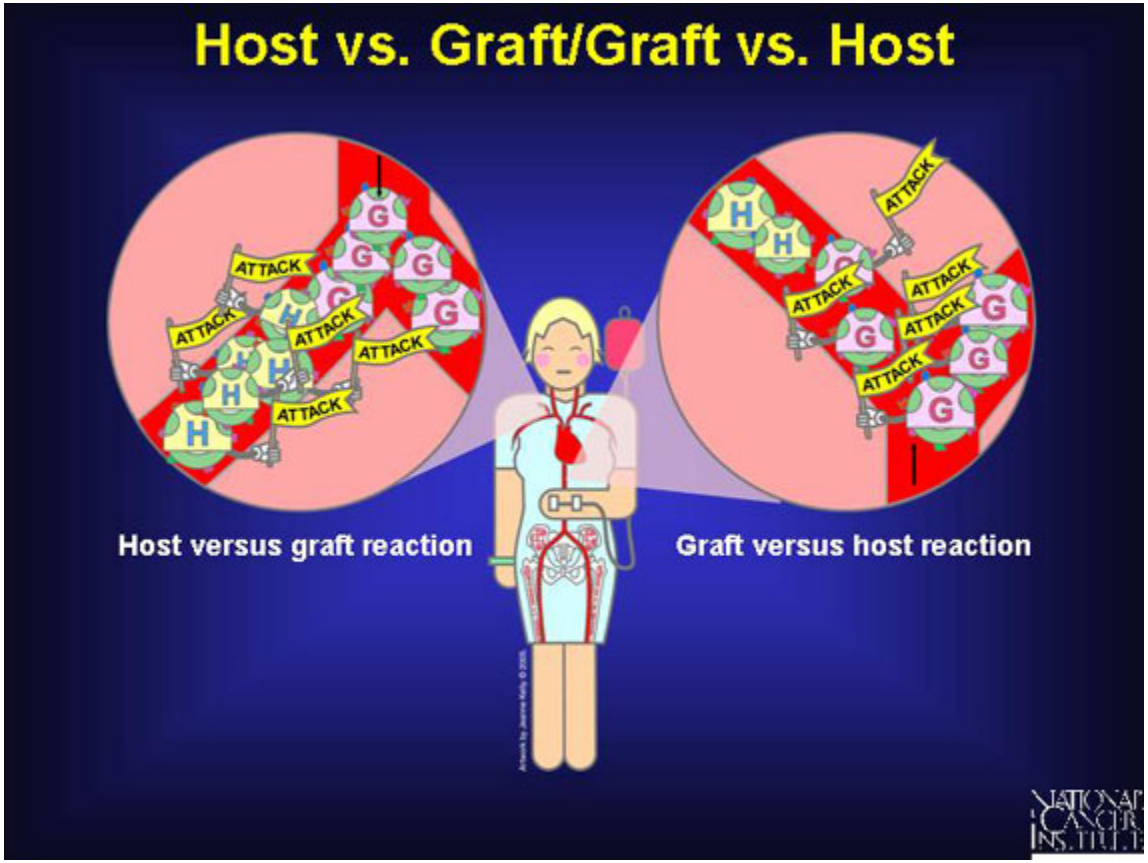
Allogeneic Stem Cell Transplant Procedure Overview



Graft vs Host Disease (GVHD)



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New Directions in Blood Cancer Treatment

Targeted Therapy:

-blocks specific proteins in the cell growth and DNA replication pathway

Immunotherapy

-Antibodies & Antibody conjugates

-Stimulating patient's immune system to fight cancer

-Checkpoint Inhibitors

-Programming patient's immune system towards their blood cancer

-Chimeric Antigen Receptor T-Cells (CAR-T cells)

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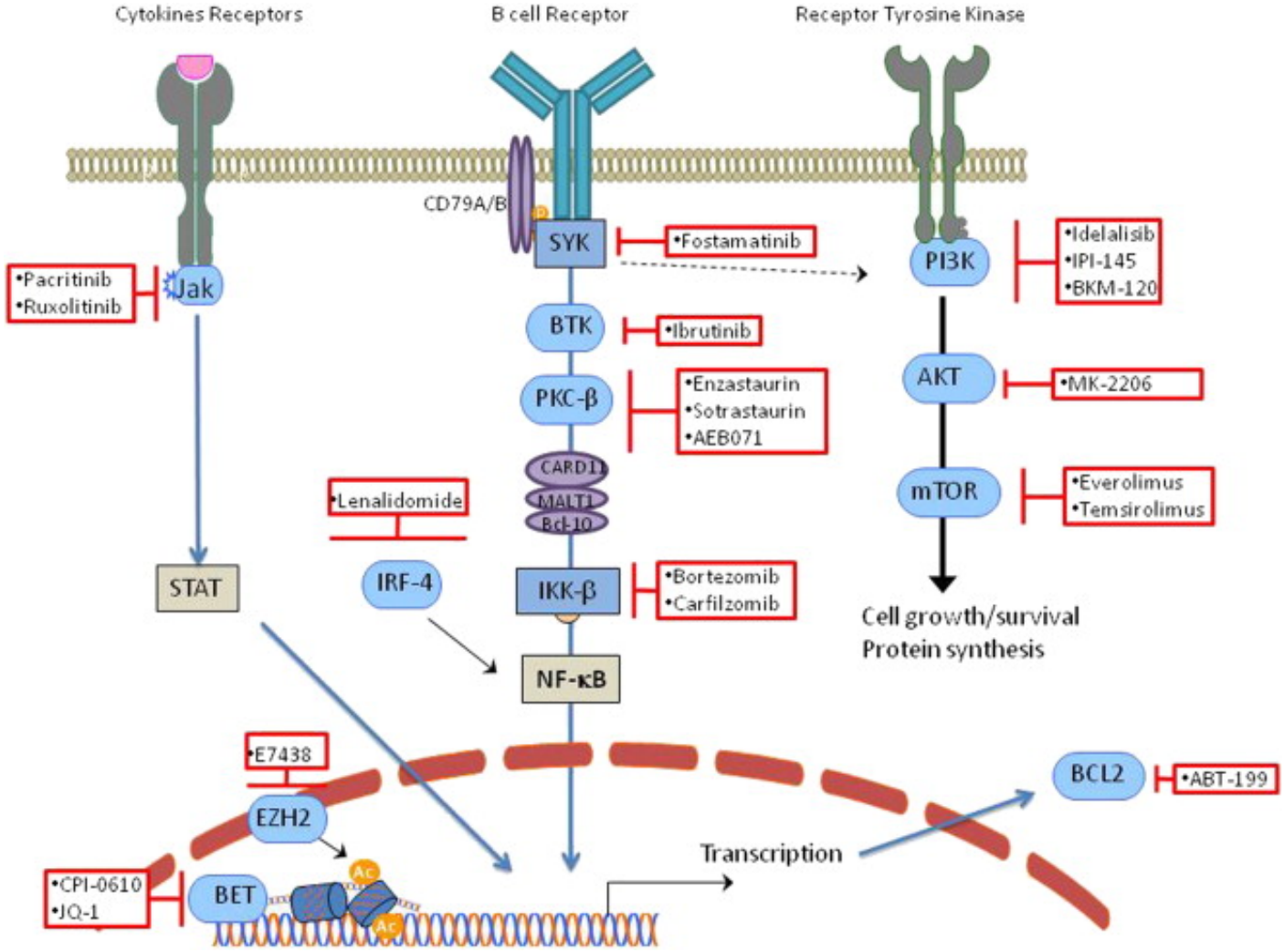
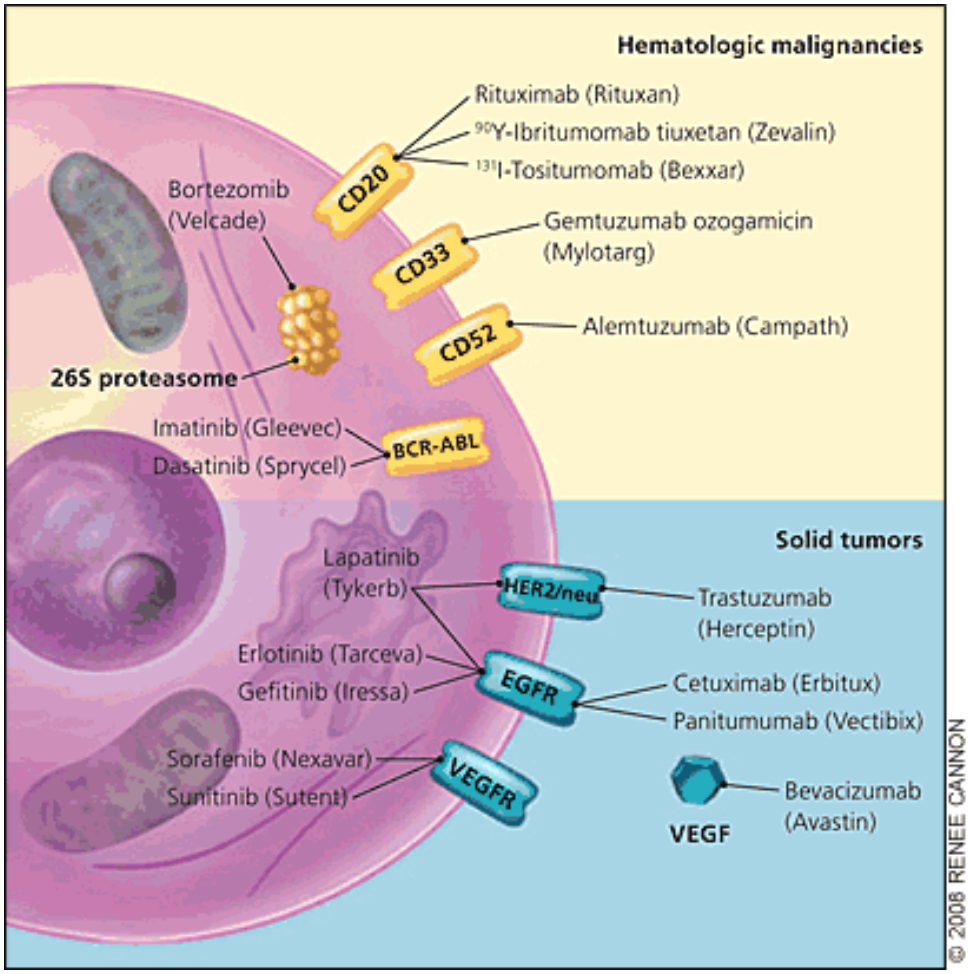
Targeted Therapy



Immunotherapy- Antibodies



Surface proteins targeted by immunotherapy

- Naked monoclonal antibodies (mAbs)
- Conjugated mAbs
  - Radioisotopes
  - Drugs
  - Toxins

Rituximab (Rituxan)

Monoclonal antibody against CD20

The first monoclonal antibody approved for use in cancer patients (1997)

Given once per week for 4 or 8 weeks or in combination with standard chemotherapy

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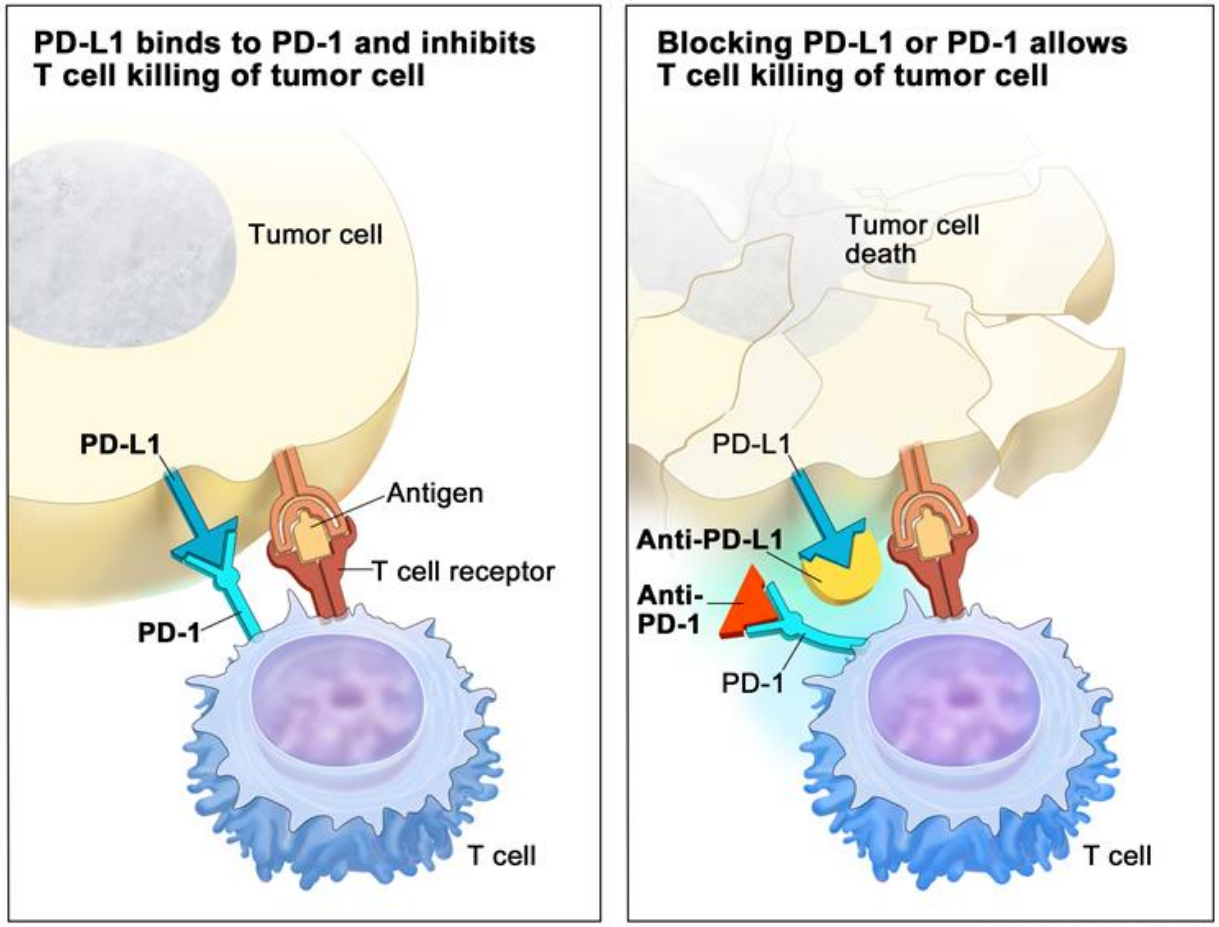
Immunotherapy-
Stimulating patient immune system



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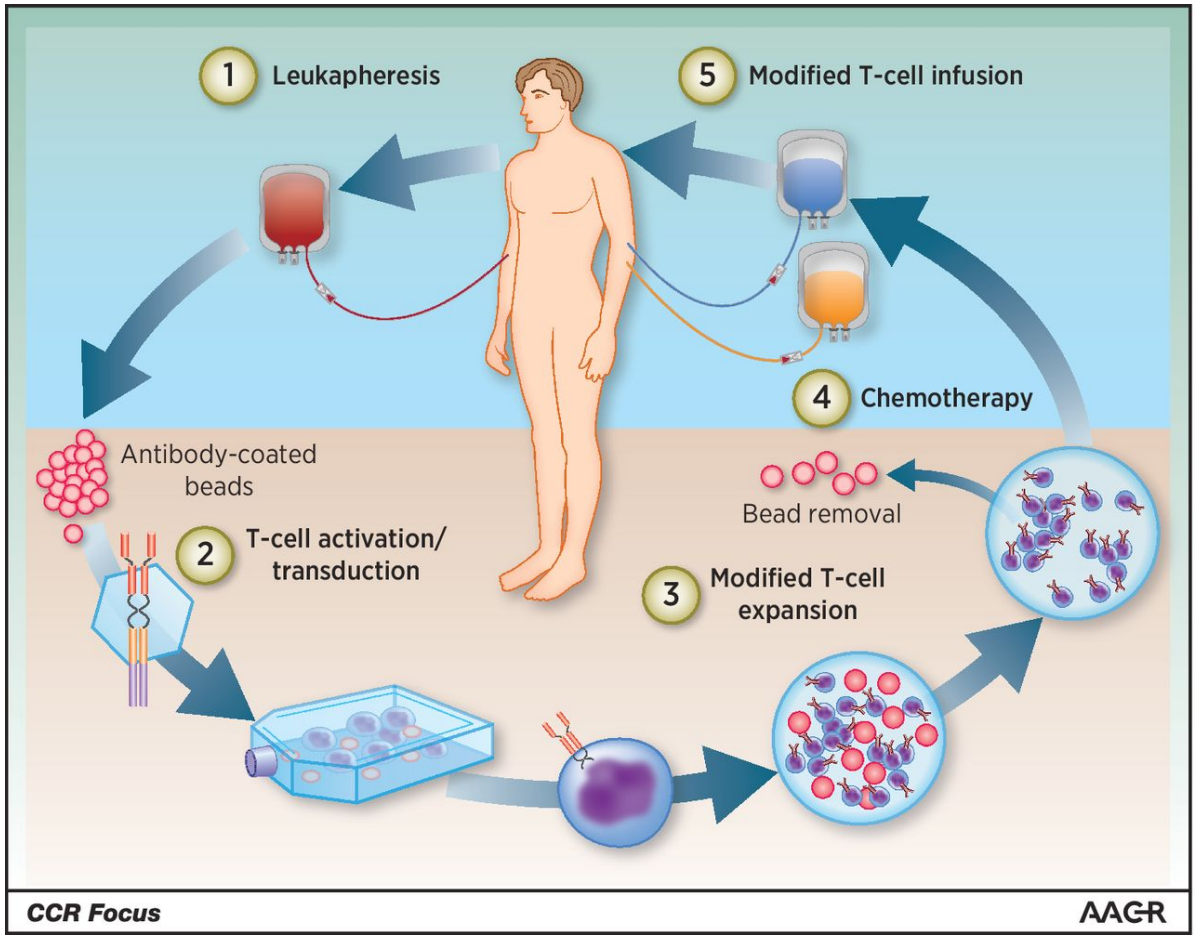
Immunotherapy-

Programming patient immune system to fight blood cancer



CAR-T Cells- Patient T-cells collected, genetically engineered to recognize your cancer better and kill it

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CAR-T Cells pending FDA Approval in ALL

Emily Whitehead, 12, and her parents, Tom and Kari Whitehead, appeared at an F.D.A. hearing on Tuesday about a treatment for leukemia that had saved Emily's life. CreditT.J. Kirkpatrick for The New York Times

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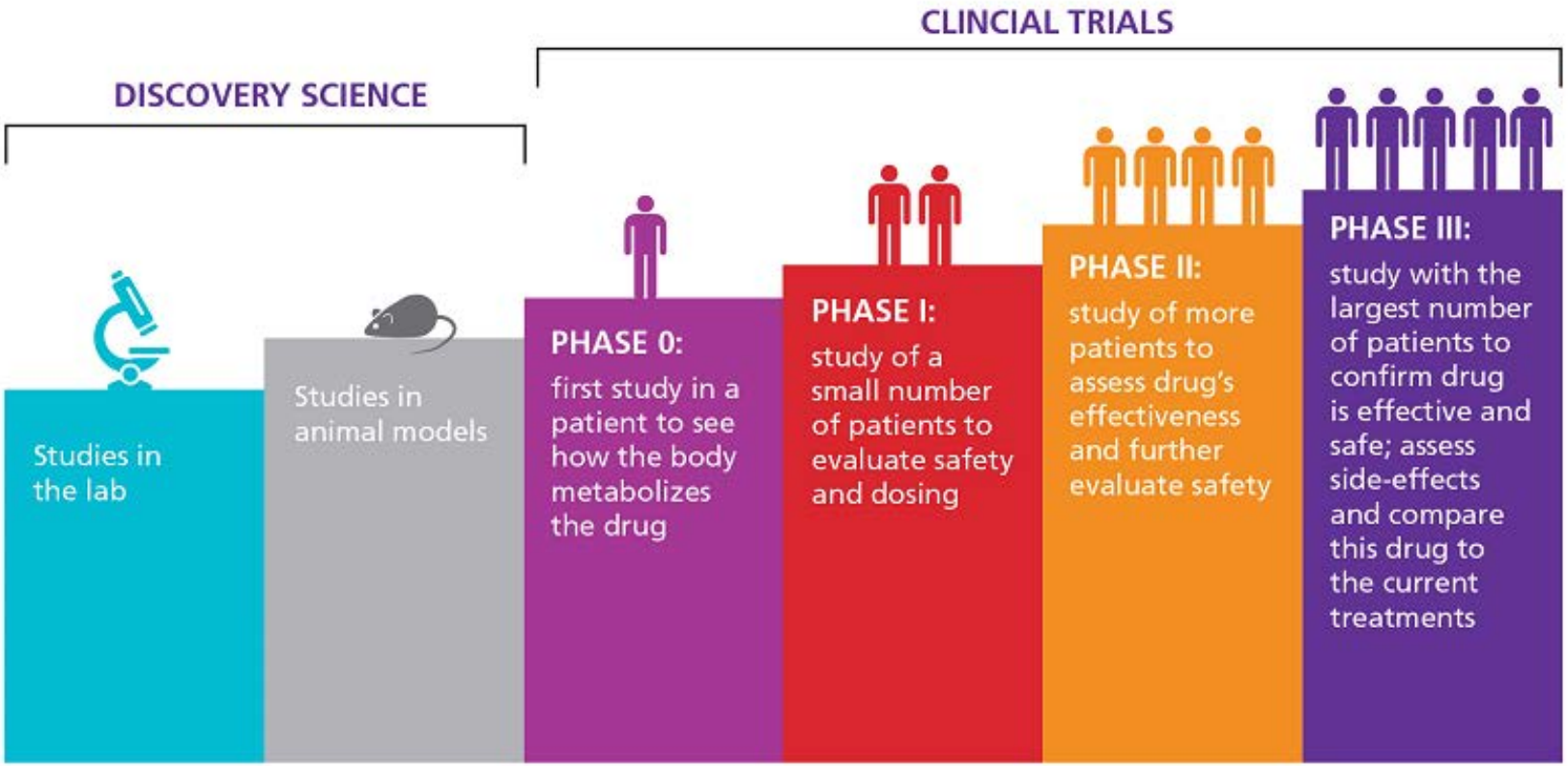
Clinical Trials



http://www.abta.org/about-us

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Why Consider a Clinical Trial

May offer additional or better options than standard therapy

Risks must be weighed against potential benefits

Understanding clinical trials

- Animal studies
- Phase I: tests dose and side effects
- Phase II: tests effectiveness in a specific tumor
- Phase III: compares standard therapy to new therapy
- FDA Approval: commercially available

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Key Questions to Ask Your Doctor

What type of blood cancer do I have? What is the specific subtype?

Is it indolent or aggressive?

What is the stage and genetics of my disease?

What are my treatment options?

What side effects may I experience and how can I deal with them?

Are there any clinical trials that I might benefit from, now or in the future?

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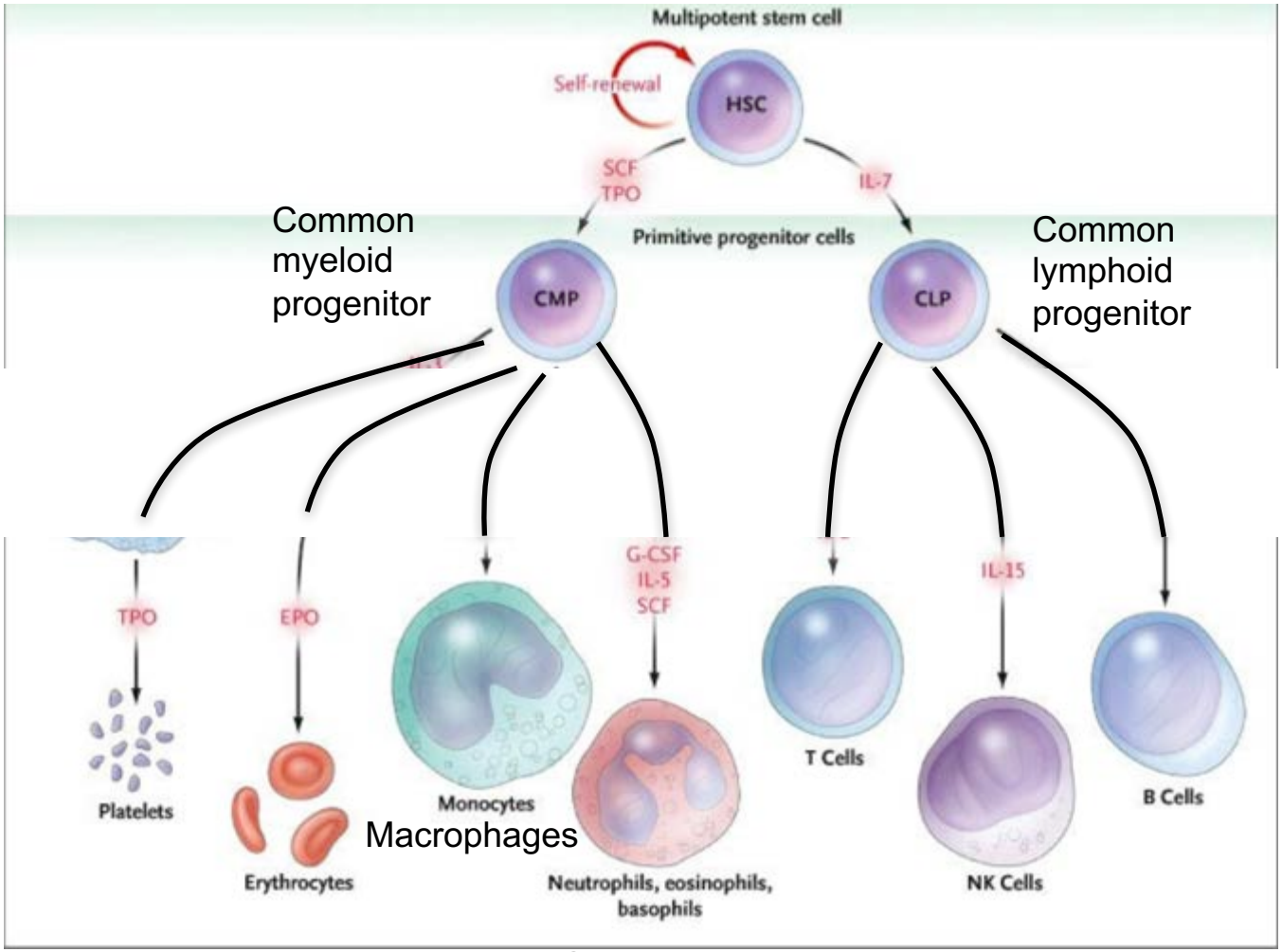
fighting blood cancers

someday is today®

Thank You



Common myeloid progenitor

Common lymphoid progenitor

Granulocytes

Adapted from Kaushansky K *NEJM*. 2006